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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/646,267 | 08/22/2003 | Kathryn Lindsay Ball | CCI-007USDV | 9453 |

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| EXAMINER | |
|---|---|
| LUKTON, DAVID | |
| **ART UNIT** | **PAPER NUMBER** |
| 1654 | |

DATE MAILED: 11/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/646,267 | BALL ET AL. | |
| | Examiner | Art Unit | |
| | David Lukton | 1654 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-8 and 11-13* is/are pending in the application.

4a) Of the above claim(s) *6,7 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Pursuant to the directives of the response filed 9/11/06, claims 1, 4, 12 have been amended, and claim 13 added. Claims 1-8, 11-13 are now pending.

Applicants' election of Group III (claims 1-5, 8, 11-12) is acknowledged. Also acknowledged is the elected "substance" which is a peptide that consists of residues 16-35 of $p21^{WAF}$, and which is sequence ID NO: 2, which in turn is the following:

KACRRLFGPVDSEQLSRDCD

The previous species elections also remain in force, i.e., the G1 cdk is cdk4; the "substance" referred to in line 2 of claim 1 is a single pure compound; and Rb phosphorylation as the specific "activity" of the G1 cdk that is to be inhibited. Claims 1-5, 8, 11, 12 are examined in this Office action; claims 6, 7 and 13 are withdrawn from consideration, as these claims do not encompass the elected species.

✧

Claims 1-5, 8, 11, 12 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites following:

> "A method of inhibiting ... comprising contacting ...with a substance which is ... a peptide fragment..., the peptide fragment ... coupled to a non-peptidyl coupling partner..."

The issue here concerns the relationship between the phrase "peptide fragment" and the phrase "the peptide fragment ... coupled to a non-peptidyl coupling partner...". At first blush, the term "wherein" would seem to be implied, i.e., the following:

> A method of inhibiting ... comprising contacting ...with a substance which is ... a peptide fragment..., **wherein** the peptide fragment is coupled to a non-peptidyl coupling partner

However, this appears not to be intended. The following language is offered for applicants' consideration; it does not necessarily overcome all issues, but it does constitute a step towards greater clarity:

*A method of inhibiting ... comprising contacting ...with a substance which is selected from the group consisting of:*

*(a) a fragment of 40 amino acids or less of p21;*

*(b) a derivative of a fragment of 40 amino acids or less of p21;*

*(c) a fragment of 40 amino acids or less of p21 coupled to a non-peptidyl carrier;*

*(d) a derivative of a fragment of 40 amino acids or less of p21, wherein said derivative of a fragment is coupled to a non-peptidyl carrier;*

*(e) a fragment of 40 amino acids or less of p21 coupled to a non-p21 peptide sequence; or*

*(f) a derivative of a fragment of 40 amino acids or less of p21, wherein said derivative of a fragment is coupled to a non-p21 peptide sequence...*

✧

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. §102(a) as being anticipated by Ball (*Current Biology* **7**, 71-80, 1996)

Ball discloses the invention substantially as claimed.

The issue here is that the priority documents have not been received, and are not present in the patent file (SN 09/180269). The assumption is that U.K. applications 9609521.1 and 9621314.5 describe an invention that is different from that which is now claimed. It is suggested that applicants provide a copy of the priority documents.

✧

The following is a quotation of 35 USC. §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as

set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claim 1-3 are rejected under 35 U.S.C. §103 as being unpatentable over Nakanishi (*EMBO Journal* **14**(3), 555-63, 1995).

Nakanishi discloses (page 560, col 2) that peptides containing the following sequence inhibit cyclin-dependent kinases:

WMNFDFXXXXPLEGXXXWXXV

The issue here is that instant claim 1 does not actually require that the peptide in question contain the subsequence RRyFz.

Claim 1 is drawn to the following:

> A method of inhibiting ... comprising contacting ...with a substance which is ... a derivative thereof..."

Thus, claim permits, in essence, that the practitioner use one of the following:

(a) a fragment of p21, wherein the fragment contains the subsequence RRyFz.

(b) a derivative of a fragment of p21, wherein the fragment contains the subsequence RRyFz;

(c) a fragment of p21 coupled to a carrier (wherein the fragment contains the subsequence RRyFz);

(d) a derivative of a fragment of p21 coupled to a carrier

Thus, when one is using a fragment of p21, it may be true that the subsequence RRyFz must be present, but when one is using a "**derivative** of a fragment", it is only the fragment that must contain the subsequence RRyFz, and not the derivative of the fragment.

This ground of rejection is directed at "derivatives of fragments", as well as "derivatives of fragments" that are coupled to carriers.

Thus, the claims are rendered obvious.

✦

Claims 1-3 are rejected under 35 U.S.C. §103 as being unpatentable over Chen, J. (*Molecular & Cellular Biology* **16**(9) 4673-4682, 1996).

Chen discloses (page 4674, col 1, paragraph 10) the following peptide:

ACRRLFGPVDSE

Chen also discloses that this, and other peptides inhibit cyclin dependent kinases.

Thus, the claims are rendered obvious.

[Applicants' priority claim to U.K. applications 9609521.1 and 9621314.5 is noted. However, these have not been received, and so it is not possible to assess the validity of applicants' priority claim].

✦

Claims 1-3 are rejected under 35 U.S.C. §103 as being unpatentable over (a) Xiong Y (*Nature* **366**(6456), 701-4, 1993) or (b) Harper, (*Mol Biol Cell* **6**, 387-400, 1995) in view of Xiong.

Xiong and Harper both teach that p21 inhibits cyclin dependent kinases; Xiong provides the sequence of p21.

Certainly, the teachings of Harper and Xiong taken together disclose a method of inhibiting the activity of a G1 cdk by contacting the cdk with a peptide that comprises (a) a fragment of less than 40 amino acids of p21 and (b) a "carrier" peptide, which happens to be another portion of p21. This conclusion is also reached by considering Xiong by itself. As it happens, however, this particular embodiment is excluded by the claims. But what is not excluded is "non-p21 peptide sequences" that are rendered obvious by Xiong. Consider the following peptide, which is a fragment of p21 (in p21, this happens to be bonded to the C-terminus of SEQ ID NO:2 of the instant application):

ALMAGCIQEARERWNFDFVTETPLEGDFAWER

This qualifies as a "p21 carrier" and is excluded by the claims. But consider each of the following:

1 ALMXGCIQEARERWNFDFVTETPLEGDFAWER

2 ALMAGCINEARERWNFDFVTETPLEGDFAWER

3 ALMAGCIQEARERWNXDFVTETPLEGDFAWER

4 ALMAGCIQEARERWNFDFLTETPLEGDFAWER

In the first of these four sequences, "X" represents ethylglycine. The peptide chemist of ordinary skill would have expected that a peptide containing an alanine at a given position will exhibit substantially the same activity as an otherwise identical peptide containing ethylglycine [*In re Shetty* (**195** USPQ 753); *In re Hass & Susie* (**60** USPQ 544)]. At the same time, this sequence would qualify as a "non-p21 carrier". Consider next the second of the four sequences. In this case, the glutamine has been replaced with asparagine. Again, this would qualify as a "non-p21 carrier". Similar to the foregoing, in the third sequence, a phenthylglycine replaces phenylalanine, and in the fourth, a leucine replaces a valine. Thus, there are a number of peptides which are rendered obvious by Xiong, but which, at the same time, meet the requirement for a "non-p21 carrier". Thus, the claims are rendered obvious.

✦

Claim 1 is rejected under 35 U.S.C. §103 as being unpatentable over Lin (*Mol Cell Biol* 16, 1786, 1996)

Lin discloses inhibition of cdk's by p21; also disclosed, however, is inhibition of cdk's by peptides which are mutants of p21. As such, the limitation of a "non-p21 sequence" is met by the reference.

Thus, the claim is rendered obvious.

✧

Claims 1 and 5 are rejected under 35 U.S.C. §103 as being unpatentable over Toyoshima, (*Cell* **78**, 67-74, 1994).

Toyoshima discloses inhibition of cdk's by p27.

The issue here is that the term "fragment" in instant claim 1 could mean just one single amino acid; thus, any amino acid that is present in p21 would qualify. As such, nearly any peptide that inhibits a G1 cdk would be encompassed by the claims. But even if applicants were to amend claim 1 to require that the "substance" in question contain a tetrapeptide subsequence of p21, the requirements of such a claim would be met by Toyoshima. For example, the peptide disclosed on page 68 (figure 1) of Toyoshima contains the pentapeptide LFGPV; this pentapeptide is also contained within p21. Similarly, the Toyoshima peptide contains the subsequence PLEG which is also contained within p21. This ground of rejection is directed at the subgenus of claim 1 which

is drawn to a fragment of 40 amino acids or less of p21 that is coupled to a non-p21 peptide sequence.

Thus, the claims are rendered obvious.

✧

Reference A5 was stricken from the IDS because of the absence of a translation. The remaining references that were stricken were so treated because they have not been received, and are not present in the parent file.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (571)272-0562. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

DAVID LUKTON, PH.D.
PRIMARY EXAMINER